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Case Report

Progressive supranuclear palsy: A case report and brief review of the literature ☆,☆☆

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ABSTRACT

Atypical Parkinsonian syndromes are a subset of progressive neurodegenerative disorders that present with signs of Parkinson's disease. However, due to multisystem degeneration, the atypical Parkinsonian syndromes have additional symptoms that are often referred to as Parkinson-plus syndromes. The most well-studied subsets include progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD), and Lewy body dementia. Specifically, progressive supranuclear palsy is a tauopathy neurodegenerative disorder that presents with parkinsonism symptoms along with postural instability, vertical saccade, and vertical gaze palsy. Here, we present a case of PSP and provide a brief review of the literature.

Introduction

Atypical Parkinsonian syndromes are a subset of progressive neurodegenerative disorders that present with signs of Parkinson's disease. Similar to Parkinson's disease, these neurodegenerative disorders are caused by protein deposits in brain tissue. The pathogenesis of these protein deposits is unclear, but advanced age is suspected to play a role [1]. There is also ongoing research to look for atypical infectious agents, random genetic agents, and specific environmental toxins that may increase the collection of protein deposits [2].

However, while these conditions involve multisystem degeneration, Parkinson's disease involves degeneration of neurons found in the substantia nigra. Therefore, these disor-

Abbreviation: PSP, progressive supranuclear palsy; MSA, multiple system atrophy; CBD, corticobasal degeneration; SCA, spinocerebellar ataxia; MRI, magnetic resonance imaging; PSP-RS, progressive supranuclear palsy-Richardson-Steele-Olszewski; PSP-P, progressive supranuclear palsy parkinsonism variant; PAGF, progressive supranuclear palsy-pure akinesia with gait freezing; TCA, tricyclic antidepressants; GSK3b, glycogen synthase kinase 3 beta; DAT, dopamine transporter; FDG-PET, fluorodeoxyglucose positron emission tomography.

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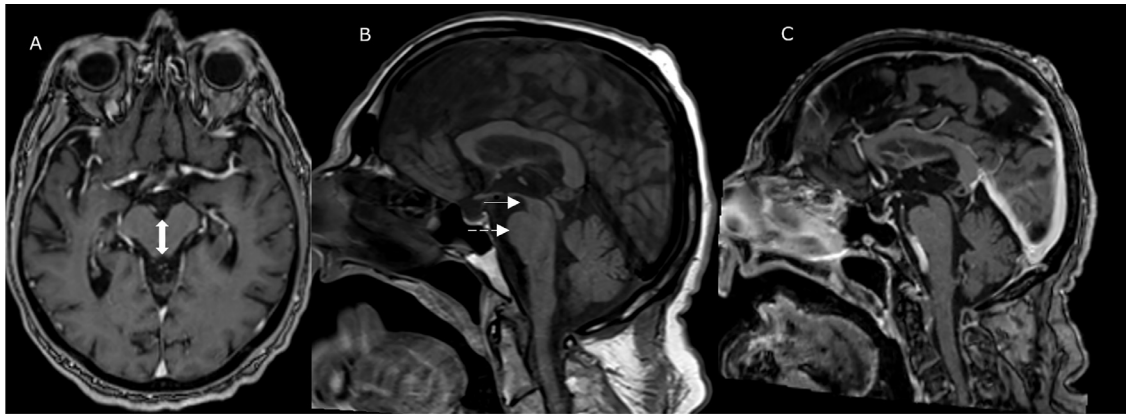

Fig. 1 – (A) Axial T1-weighted post contrast showing a reduced anteroposterior midline-midbrain diameter(arrow) and Mickey Mouse appearance. (B) Sagittal T1-weighted showing decreased midbrain (solid line arrow) to pons (dashed line arrow) area ratios and flattening of superior aspect of the midbrain resulting in the Hummingbird sign (C) Sagittal T1-weighted post contrast images showing midbrain atrophy.

ders have typical Parkinsonian symptoms such as resting tremors, bradykinesia, rigidity, and postural instability [3]. Due to multisystem degeneration, the atypical Parkinsonian syndromes have additional symptoms that are often referred to as Parkinson-plus syndromes. The most well-studied subsets include progressive supranuclear palsy (PSP), multiple system atrophy (MSA), corticobasal degeneration (CBD), and Lewy body dementia. As a result of the overlap of these syndromes and their case presentation, they are often challenging to differentiate [4].

Here, we present a case of PSP with emphasis on imaging findings and a brief review of the literature.

Case presentation

An 84-year-old male with a past medical history significant for hypertension, chronic pain, and hypothyroidism presented to the neurology clinic with restricted vertical gaze, eyelid apraxia, significant freezing, neck rigidity out of proportion to the tone in his extremities, and increased frequency of backward falls. He also has difficulty opening his eyes and has had previous eyelid lift surgery due to failing a trial of Botox treatment. Parkinson's disease was clinically suspected, further evaluation with an MRI brain was recommended and Sinemet was initiated.

There was no clinical improvement with Sinemet. MRI brain showed atrophy of the midbrain with normal findings in the basal ganglia and pons. No diffusion restriction or abnormal contrast enhancement was present. Findings favor PSP over alternative clinical diagnoses of Parkinson's disease and multiple system atrophy (Fig. 1).

Symptomatic therapy was initiated, and the patient continues to follow up with neurology on an outpatient basis.

Discussion

Progressive supranuclear palsy is the most common form of atypical parkinsonism, and current research suggests that PSP makes up 5% of patients presenting with parkinsonism and has an incidence of 0.005%. The average age of onset of symptoms is 63 and patients have a mean survival of 7 years after diagnosis [5]. The key symptoms of the disease include early postural instability, vertical saccade, and vertical gaze palsy. These patients also have a characteristic "procerus sign," which is a vertical wrinkling of the forehead that results in a worried facial expression [3]. PSP has a characteristic broad-based gait with extended knees and abducted arms that result in a high fall risk [6]. As a result, these patients have an increased backward fall risk compared to those with other syndromes [7].

PSP has also been categorized into a variety of subtypes depending on the clinical presentation and pathological results [8]. The most common subtype that makes up more than 50% of the cases is the classic type, otherwise known as the PS—Richardson-Steele-Olszewski (PSP-RS) [7]. This subtype has been categorized by primary clinical presentation with oculomotor dysfunction and postural instability before the development of Parkinsonian symptoms. The second most common subtype is the PSP-Parkinsonism variant (PSP-P), which is seen in up to one-third of PSP cases [9]. This subtype is typically not associated with degeneration of the midbrain tegmentum in the initial stages. There are also other rare subtypes that cumulatively makeup 5% of PSP cases. These include the PSP-pure akinesia with gait freezing (PAGF) and the cortical PSP variants.

The distinction between subtypes is clinically important, as the subtypes all have differing prognoses. The PSP-P and PAGF subtypes have been associated with a more benign course and the patients have a life expectancy greater than 10 years. This is due to the symptoms being isolated to the brainstem, along with the conditions having a lower tau burden [10].

In contrast, the PSP-RS and other variants have more cortical involvement and a poorer prognosis with a life expectancy of less than 7 years [11].

Currently, there is no known cure for PSP. The treatment involves symptomatic relief for abnormal eye movements, depression, and parkinsonism, using medications such as dopamine agonists and dopa decarboxylase inhibitors for Parkinsonian symptoms. The research has shown that Levodopa can reduce Parkinsonian symptoms in up to 50% of patients and result in modest improvement in physical status [12]. Patients also benefit from botulinum toxin injections to help with supranuclear vertical gaze palsy [13]. While traditional depression medications have been shown to help with mood in PSP patients, case reports have indicated that TCAs may provide a good response to depression [14]. However, these patients are also often prescribed methylphenidate, as none of the antidepressants help with symptoms of apathy that are seen in these patients [15]. Due to PSP disorders having neurodegeneration secondary to misfolded tau proteins, current research is looking at targeted molecular therapy and genetic therapies for improving symptoms [16]. In particular, the key enzymatic step in the hyperphosphorylation of tau involves glycogen synthase kinase 3 beta (GSK3b), so new drugs such as Tideglusib and Davunetide, which inhibit this kinase, are being studied to help reduce aggregation of misfolded proteins [17].

Since current treatment of PSP is mainly supportive, it is essential to have a prompt diagnosis of the disease and early intervention. Imaging is helpful to achieve an early diagnosis. The key radiographic findings seen in PSP include midbrain atrophy, which can be quantified through the magnetic resonance Parkinsonism index, calculated from several measurements of the images as described in the reference [18]. The patient may also have the hummingbird sign, which is a concave contour of the superior midbrain seen in the midsagittal view [19]. The hummingbird sign has a specificity of 99.5% but a suboptimal sensitivity of 51.6%. Hence, the hummingbird sign is unable to differentiate between PSP, MSA, and Parkinson's Disease [20]. PSP is also characterized by sparing of the transverse pontocerebellar tracts, which are damaged in conditions such as MSA and SCA [21]. As a result of pontocerebellar tract degeneration, MSA and SCA can result in the classic hot cross bun sign that is not seen in PSP [22].

While imaging helps suggest a diagnosis, there is limited use for imaging in confirming the diagnosis in patients presenting with Parkinsonian symptoms [23]. In fact, no neuroimaging modality is currently recommended for use in routine clinical practice, because these patients often have signs on imaging that are difficult to characterize [24]. However, these patients can still benefit from MRI imaging due to the identification of characteristic findings for Parkinson's disease. MRI imaging can also be used to rule out structural causes for Parkinsonian symptoms, such as a lesion or vascular deficit that could be contributing to the patient's symptoms [25]. Similarly, imaging can be used to help differentiate Parkinson's disease from atypical Parkinsonian syndromes, which may have their own suggestive imaging findings such as the hot cross bun or hummingbird signs. Lastly, the imaging can be used to quantify cerebral volume loss that is seen with Parkinson's so as to monitor the progression of the disease [24].

The characteristic imaging finding of Parkinson's disease on T2 MRI imaging is the loss of dorsal hyperintensity within the substantia nigra, otherwise known as the absent swallow tail sign. Current research suggests that a portion of the swallow tail sign overlaps with Nigrosome-1, making it a partial contributor to this diagnostic region [26]. Nigrosome-1 is the most dorsal of 5 regions, labeled Nigrosomes 1-5, of concentrated dopaminergic neurons in the substantia nigra pars compacta, and it has a proportionately low iron concentration. The increase in iron content within all nigrosomes is associated with Parkinson's disease and is responsible for the hypointensity of Nigrosome-1 in T2 imaging and hyperintensity of compact and reticular parts of the substantia nigra in T1 imaging that is best appreciated on 3T MRI [27]. There has also been recent interest in Neuromelanin imaging, especially at ultra-high-field strength [28]. These findings are different from what we see with atypical Parkinsonian syndromes, such as PSP.

Other than conventional MRI imaging, there has been recent work in molecular imaging to help diagnose Parkinson's disease and PSP. There is new research with fluorodeoxyglucose positron emission tomography (FDG-PET) to help suggest the diagnosis of PSP [29]. For example, patients with PSPS-RS often have frontal and midbrain hypometabolism and these findings, along with the corresponding clinical symptom, can help guide the diagnosis [30]. Additionally, the 23I-ioflupane DaT-SCAN has also shown promising results in highlighting a reduction in the function of dopamine transporters (DAT). The initial research has shown that the function of the DAT transporter was reduced in PS patients in comparison to Parkinson's disease [31]. While these results have shown high sensitivities with the test to diagnose Parkinsonian syndromes, it is not without limitations. The test has limited accuracy in differentiating between Parkinson's disease, MSA, and PSP [14]. The definite diagnosis of PSP still requires pathological support, as the disorder is a tauopathy: a neurodegenerative disorder characterized by tau deposits in the brain [32].

In conclusion, differentiating between Parkinson's disease and atypical Parkinsonian syndrome such as PSP may be difficult. While the confirmation of either of these diagnoses is not possible based only on medical imaging, new advancements in MRI and nuclear medicine imaging can help guide the diagnosis. In our case, the hummingbird sign was also present in this case of PSP.

Patient consent

Written consent was obtained for the publication of the current case. No patient identifiers disclosed.

REFERENCES

[1] Golbe LI, Davis PH, Schoenberg BS, Duvoisin RC. Prevalence and natural history of progressive supranuclear palsy. Neurology 1988;38(7):1031–4. doi:10.1212/wnl.38.7.1031.

[2] Litvan I, Lees PSJ, Cunningham CR, Rai SN, Cambon AC, Standaert DG, et al. Environmental and occupational risk factors for progressive supranuclear palsy: Case-control study. Mov Disord 2016;31(5):644–52. doi:10.1002/mds.26512.
[3] McFarland NR. Diagnostic approach to atypical parkinsonian syndromes. Continuum (Minneapolis, Minn.) 2016;22(4):1117–42 Movement Disorders. doi:10.1212/CON.0000000000000348.
[4] Deutschländer AB, Ross OA, Dickson DW, Wszolek ZK. Atypical Parkinsonian syndromes: a general neurologist's perspective. Eur J Neurol 2018;25(1):41–58. doi:10.1111/ene.13412.
[5] Golbe LI. Progressive supranuclear palsy. Semin Neurol 2014;34(2):151–9. doi:10.1055/s-0034-1381736.
[6] Egerton T, Williams DR, Iansek R. Comparison of gait in progressive supranuclear palsy, Parkinson's disease, and healthy older adults. BMC Neurol 2012;12:116. doi:10.1186/1471-2377-12-116.
[7] Williams DR, Lees AJ. Progressive supranuclear palsy: clinicopathological concepts and diagnostic challenges. Lancet Neurol 2009;8(3):270–9. doi:10.1016/S1474-4422(09)70042-0.
[8] Coughlin DG, Litvan I. Progressive supranuclear palsy: advances in diagnosis and management. Parkinsonism & Relat Disord 2020;73:105–16. doi:10.1016/j.parkreldis.2020.04.014.
[9] Williams DR, de Silva R, Paviour DC, Pittman A, Watt HC, Kilford L, et al. Characteristics of two distinct clinical phenotypes in pathologically proven progressive supranuclear palsy: Richardson's syndrome and PSP-parkinsonism. Brain 2005;128(Pt 6):1247–58. doi:10.1093/brain/awh488.
[10] Williams DR, Holton JL, Strand C, Pittman A, de Silva R, Lees AJ, et al. Pathological tau burden and distribution distinguishes progressive supranuclear palsy-parkinsonism from richardson's syndrome. Brain 2007;130(Pt 6):1566–76. doi:10.1093/brain/awm104.
[11] Alster P, Madetko N, Koziorowski D, Friedman A. Progressive supranuclear palsy-parkinsonism predominant (PSP-P)-a clinical challenge at the boundaries of PSP and Parkinson's disease (PD). Front Neurol 2020;11:180. doi:10.3389/fneur.2020.00180.
[12] Lubarsky M, Juncos JL. Progressive supranuclear palsy: a current review. Neurologist 2008;14(2):79–88. doi:10.1097/NRL.0b013e31815cffc9.
[13] Piccione F, Mancini E, Tonin P, Bizzarini M. Botulinum toxin treatment of apraxia of eyelid opening in progressive supranuclear palsy: report of two cases. Arch Phys Med Rehabil 1997;78(5):525–9. doi:10.1016/s0003-9993(97)90169-6.
[14] Pagano G, Niccolini F, Politis M. Imaging in Parkinson's disease. Clin Med (London, England) 2016;16(4):371–5. doi:10.7861/clinmedicine.16-4-371.
[15] Chatterjee A, Fahn S. Methylphenidate treats apathy in Parkinson's disease. J Neuropsychiatry Clin Neurosci 2002;14(4):461–2. doi:10.1176/jnp.14.4.461.
[16] Sun J, Roy S. Gene-based therapies for neurodegenerative diseases. Nat Neurosci 2021;24(3):297–311. doi:10.1038/s41593-020-00778-1.
[17] Boeve BF. Progressive supranuclear palsy. Parkinsonism Relat Disord 2012;18(Suppl 1):192. doi:10.1016/S1353-8020(11)70060-8.
[18] Quattrone A, Nicoletti G, Messina D, Fera F, Condino F, Pugliese P, et al. MR imaging index for differentiation of progressive supranuclear palsy from Parkinson disease and the Parkinson variant of multiple system atrophy. Radiology 2008;246(1):214–21. doi:10.1148/radiol.2453061703.
[19] Virhammar J, Blohmé H, Nyholm D, Georgiopoulos C, Fällmar D. Midbrain area and the hummingbird sign from brain MRI in progressive supranuclear palsy and idiopathic normal pressure hydrocephalus. J Neuroimag 2022;32(1):90–6. doi:10.1111/jon.12932.
[20] Mueller C, Hussl A, Krismer F, Heim B, Mahlknecht P, Nocker M, et al. The diagnostic accuracy of the hummingbird and morning glory sign in patients with neurodegenerative parkinsonism. Parkinsonism Relat Disord 2018;54:90–4. doi:10.1016/j.parkreldis.2018.04.005.
[21] Ando S, Kanazawa M, Onodera O. Progressive supranuclear palsy with predominant cerebellar ataxia. J Mov Disord 2020;13(1):20–6. doi:10.14802/jmd.19061.
[22] Way C, Pettersson D, Hiller A. The 'hot cross bun' sign is not always multiple system atrophy: etiologies of 11 cases. J Mov Disord 2019;12(1):27–30. doi:10.14802/jmd.18031.
[23] Politis M. Neuroimaging in Parkinson disease: from research setting to clinical practice. Nat Rev Neurol 2014;10(12):708–22. doi:10.1038/nrneurol.2014.205.
[24] Bae YJ, Kim J, Sohn C, Choi J, Choi BS, Song YS, et al. Imaging the substantia nigra in Parkinson's disease and other Parkinsonian syndromes. Radiology 2021;300(2):260–78. doi:10.1148/radiol.2021203341.
[25] Rowe JB, Holland N, Rittman T. Progressive supranuclear palsy: diagnosis and management. Pract Neurol 2021;21(5):376–83. doi:10.1136/practneurol-2020-002794.
[26] Brammerloh M, Kirilina E, Alkemade A, Bazin P, Jantzen C, Jäger C, et al. Swallow tail sign: revisited. Radiology 2022;305(3):674–7. doi:10.1148/radiol.212696.
[27] Aludin S, Schmill LA. MRI signs of Parkinson's disease and atypical parkinsonism. [Magnetresonanztomografische Zeichen des idiopathischen Parkinson-Syndroms sowie atypischer Parkinson-Syndrome]. RoFo 2021;193(12):1403–10. doi:10.1055/a-1460-8795.
[28] Lakhani DA, Middlebrooks EH. 7-T neuromelanin and R2* MRI in Parkinson disease. Radiology 2022;305(2):296. doi:10.1148/radiol.220230.
[29] Ogawa T, Fujii S, Kuya K, Kitao S, Shinohara Y, Ishibashi M, et al. Role of neuroimaging on differentiation of Parkinson's disease and its related diseases. Yonago Acta Medica 2018;61(3):145–55. doi:10.33160/yam.2018.09.001.
[30] Armstrong MJ. Progressive supranuclear palsy: an update. Curr Neurol Neurosci Rep 2018;18(3):12–15. doi:10.1007/s11910-018-0819-5.
[31] Roussakis A, Piccini P, Politis M. Clinical utility of DaTscan™ (123I-ioflupane injection) in the diagnosis of Parkinsonian syndromes. Degener Neurol Neuromusc Dis 2013;3:33–9. doi:10.2147/DNND.S19807.
[32] Pandey S. Hummingbird sign in progressive supranuclear palsy disease. J Res Med Sci 2012;17(2):197–8.